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Patients with Prior Fractures Have an Increased Risk of Future Fractures: A Summary of the Literature and Statistical Synthesis*

CAROLYN M. KLOTZBUECHER, PHILIP D. ROSS, PAMELA B. LANDSMAN, THOMAS A. ABBOTT III, and MARC BERGER

ABSTRACT

Numerous studies have reported increased risks of hip, spine, and other fractures among people who had previous clinically diagnosed fractures, or who have radiographic evidence of vertebral fractures. However, there is some variability in the magnitudes of associations among studies. We summarized the literature and performed a statistical synthesis of the risk of future fracture, given a history of prior fracture. The strongest associations were observed between prior and subsequent vertebral fractures; women with preexisting vertebral fractures (identified at baseline by vertebral morphometry) had approximately 4 times greater risk of subsequent vertebral fractures than those without prior fractures. This risk increases with the number of prior vertebral fractures. Most studies reported relative risks of approximately 2 for other combinations of prior and future fracture sites (hip, spine, wrist, or any site). The confidence profile method was used to derive a single pooled estimate from the studies that provided sufficient data for other combinations of prior and subsequent fracture sites. Studies of peri- and postmenopausal women with prior fractures had 2.0 (95% CI = 1.8, 2.1) times the risk of subsequent fracture compared with women without prior fractures. For other studies (including men and women of all ages), the risk was increased by 2.2 (1.9, 2.6) times. We conclude that history of prior fracture at any site is an important risk factor for future fractures. Patients with a history of prior fracture, therefore, should receive further evaluation for osteoporosis and fracture risk. (J Bone Miner Res 2000;15:721–739)

Key words: osteoporosis, fractures, fracture risk

INTRODUCTION

OSTEOPOROSIS IS A major public health problem, occurring in every population and geographic area studied.[1–4] It affects an estimated 20 million people (26%) over the age of 45 in the United States, which resulted in $13.8 billion in health care costs in 1995.[1,5–8] Osteoporosis is defined as a systemic disease, characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk.[4,9,10] Most fractures in the elderly are related to osteoporosis;[11] common fracture sites include the proximal femur (hip), vertebral bodies, distal forearm, proximal humerus, and ribs.[4,10,12] It is estimated that more than 40% of postmenopausal women, and approximately 25 to 33% of men will eventually experience osteoporotic fractures.[3,13,14] Many people are not aware of the risk

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Merck & Company, Inc., West Point, Pennsylvania, and Rahway, New Jersey, U.S.A.

factors for and consequences of osteoporosis.[13] Given that there are no symptoms before fracture, it is important that physicians and patients recognize the risk factors.

Although history of prior fracture has been associated with increased risk of subsequent fractures in the literature, there has been no systematic review to summarize the magnitude and consistency of these associations by location of prior or subsequent fracture. Therefore, the goals of the current study were to summarize the literature, and to examine whether risk varies by location of prior fracture or by location of subsequent fracture.

MATERIALS AND METHODS

A Medline search was performed using the search terms "osteoporosis" and "fractures" to identify all articles in English from January 1966 up to September 1999. A total of 3576 articles were identified; those that appeared to be relevant, based on the titles (and abstracts when available), were retrieved. Articles that reported relative risks for associations of prior and subsequent fractures were considered for inclusion here. Abstracts from conference proceedings were also considered, but were not searched systematically. The authors endeavored to include all possible reports, considering reports from major prospective studies of osteoporosis known to them, books and review articles on osteoporosis, and articles on risk factors for fractures. Articles listed in the bibliographies of all identified papers were also considered, and experts in the field were asked to provide citations of articles known to them.

For this report, associations with future fractures are grouped by type of preexisting fracture; the order of presentation here reflects the sequence and incidence often observed in clinical practice. Wrist and spine fractures are two of the most common osteoporotic fractures. The incidence of these two fractures begins to increase rapidly soon after menopause.[2,3,13] As such, wrist and spine fractures represent harbingers of subsequent hip fractures and additional fractures at the spine and other skeletal sites.

Details of each report identified, including study design, age range, number of observations, gender, length of follow-up, and so forth, are provided in the appendices, along with the published relative risk estimates and 95% confidence intervals (CI) where available. Some studies reported the results of subanalyses, restricted to certain age ranges or fracture sites, or adjusted for additional covariates, and these results are also tabulated.

Statistical synthesis

A statistical synthesis was performed for the prior/subsequent fracture combinations for which there were at least two publications with relative risk estimates and 95% confidence intervals (CI). Random-effects models, using the confidence profile method, were applied to derive the summary estimates of relative risk.[15,16] This model works under the assumption that the individual study results combined are a random sample of the true values in the larger population. This approach yields wider confidence intervals than produced with fixed-effects modeling, accounting for study heterogeneity.

Published results based on peri- or postmenopausal women exclusively were analyzed together (Peri-/postmenopausal); this category includes estimates based on women aged 45 years and older. The remaining published estimates, which presented results for men only, women of all ages, or men and women combined, were analyzed separately (Other); some of these studies included postmenopausal women, but did not provide separate estimates for them. Pooled relative risk estimates were calculated for each combination of prior fracture and subsequent fracture type (e.g., wrist fracture predicting subsequent hip fracture); single published values are provided when only one report was available. Pooled estimates were also calculated for more general groupings: by location of prior fracture (individual rows in the resulting summary table), by location of subsequent fracture (columns in the table), and for all rows and columns combined. Associations between prior and subsequent vertebral fractures were excluded from the row and column estimates, and are discussed separately. When multiple analyses were provided from a single study, only one value was used from each report for each combination of prior and subsequent fracture. Thus, one report could contribute to wrist fractures as predictors of all fractures as well as of hip fractures. Values adjusted for age only were used whenever possible, because most studies did not adjust for bone mineral density (BMD) or other potential confounders, and because practicing physicians are generally not able to take such factors into account. The published relative risks and 95% CI used in calculating the pooled estimates for Table 1 are tabulated in Appendix 1. Appendix 2 contains the relative risk estimates and summaries of the age range, gender distribution, sample size, and other information for individual articles, including studies and subanalyses that were not included in the pooled estimates shown in Table 1.

RESULTS

Prior wrist fracture

There were nine publications that reported associations of prior wrist fractures with subsequent fractures (Appendix 2). The study designs included cross-sectional mail surveys, and case-control and prospective cohort studies. Only one study was limited to postmenopausal women;[17] most of the other studies involved women aged 45 and older, or both men and women (including some pre- and perimenopausal women).[18–22] One study included premenopausal women as young as 20 years[23] and one studied men only.[24] Associations of similar magnitude (relative risk [RR] = 1.4 to 2.7) were reported for both men and women in each of five hip fracture studies.[17,20,21,23,25]

The studies of men[24,25] reported associations with fractures of all types (RR = 1.8 to 2.5) that were similar in magnitude to studies of women (RR = 1.5 to 2.4).[17–19,22,25] One study did not provide 95% CI,[18] leaving eight studies for pooling. Differences in the magnitudes of associations with subsequent hip versus all types of

TABLE 1. POOLED ASSOCIATIONS OF PRIOR AND SUBSEQUENT FRACTURES

Location of prior fracture	*Population*	*Location of subsequent fractures*				
		Wrist	*Vertebral*	*All (or nonspine)*	*Hip*	*Pooled*
Wrist	Peri/postmenopausal	3.3 (2.0, 5.3)[a]	1.7 (1.4, 2.1)[a]	2.4 (1.7, 3.4)[a,d]	1.9 (1.6, 2.2)	2.0 (1.7, 2.4)[d]
	Other	3.6 (1.9, 6.7)	7.2 (3.6, 14.6)	2.0 (1.7, 2.4)	1.5 (1.3, 1.7)	2.6 (1.9, 3.5)
Vertebral	Peri/postmenopausal	1.4 (1.2, 1.7)[a]	4.4 (3.6, 5.4)[d]	1.8 (1.7, 1.9)	2.3 (2.0, 2.8)	1.9 (1.7, 2.3)[b]
	Other	1.4 (1.1, 1.9)	19.0 (6.5, 55.3)	2.7 (1.8, 3.9)	2.1 (1.6, 2.7)	2.3 (1.8, 2.9)[b]
Other (all, or specific sites)	Peri/postmenopausal	1.8 (1.3, 2.4)	1.9 (1.3, 2.8)[d]	1.9 (1.3, 2.7)[d]	2.0 (1.7, 2.3)	1.9 (1.7, 2.2)[d]
	Other	—[c]	—[c]	1.4 (1.2, 1.7)	2.1 (1.2, 3.5)	1.7 (1.4, 2.2)[d]
Hip	Peri/postmenopausal	—[c]	2.5 (1.8, 3.5)	1.9 (NA)[a]	2.3 (1.5, 3.7)[a]	2.4 (1.9, 3.2)
	Other	—[c]	—[c]	2.1 (1.3, 3.4)	1.6 (1.3, 1.9)[a]	1.7 (1.4, 2.0)
Pooled	Peri/postmenopausal	1.9 (1.3, 2.8)	2.0 (1.6, 2.4)[b,d]	1.9 (1.6, 2.2)[d]	2.0 (1.9, 2.2)	2.0 (1.8, 2.1)[b,d]
	Other	2.3 (1.7, 3.3)	7.2 (3.6, 14.6)[b]	1.8 (1.6, 2.2)	1.8 (1.6, 2.2)	2.2 (1.9, 2.6)[b]

[a] Only 1 study is represented.
[b] Excludes prior vertebral fracture predicting subsequent vertebral fracture, because stronger associations were observed.
[c] No studies available; NA = no CI reported.
[d] Other relative risk estimates were reported, but were not included in the pooled estimates because measures of variability were lacking, or because estimates were biased due to differences in follow-up. See Appendix 1 for a list of the estimates that were pooled, and the corresponding references.

subsequent fractures were not remarkable, but stronger associations (RR = 3.3 to 10.7) were reported for some studies of subsequent wrist and vertebral fractures[19,25] (Table 1 and Appendix 1). The pooled estimate for all types of subsequent fracture types combined was slightly lower for peri-/postmenopausal women (RR = 2.0; 95% CI = 1.7, 2.4), compared with 2.6 (1.9, 3.5) for other studies (Table 1).

If wrist fractures are an indicator of osteoporosis, one might expect wrist fractures that occur before menopause to be weaker predictors of fractures in later life, because osteoporosis is rare before menopause, and most such fractures might be related to trauma rather than low BMD. However, there was little difference in association with all types of fractures in one study in which the prior wrist fractures occurred between ages 20–34 years (RR = 2.4 for other fractures)[19] compared with studies in which most prior wrist fractures occurred after age 45 years (RR = 1.5 to 2.1).[18,22] This finding is supported by other evidence that increased fracture risk among perimenopausal women and adolescents is associated with low bone mass.[26–28]

Prior vertebral fracture

Fifteen publications reported associations of prior vertebral fractures with subsequent fractures (Appendix 2). Seven of these studies were based on prior clinical (symptomatic) vertebral fractures[17,22,24,29–32] and the remainder were based on prior morphometric fractures identified at baseline using radiographs.[33–39,53] Morphometric fractures are diagnosed on the basis of reduced vertebral body height; approximately half of women with morphometric fractures do not report having back pain, and approximately two-thirds had not had a clinical diagnosis of fracture.[40] The age at which preexisting morphometric vertebral fractures had occurred is usually not known, except for the third of fracture cases that had been clinically diagnosed.

Most studies of prior vertebral fractures were either prospective, nested case-control, or used population-based records to compare the incidence of new fractures among cases with prior vertebral fractures to incidence rates in the community, but one study used a cross-sectional mail survey.[17] Except for one study of men,[24] and three studies that included both men and women, the remaining studies were restricted to women, and most of the women (in all studies) were postmenopausal when fractures were diagnosed.

There were no obvious differences between clinical and morphometric fractures in the magnitudes of associations with subsequent wrist, hip, or "all/other" fractures (Appendices 1 and 2). Associations with subsequent hip fractures were somewhat stronger (pooled RR = 2.3) than with all subsequent fractures combined (RR = 1.8) among peri-/postmenopausal women, but the converse was observed for other studies (Table 1). The association of prior vertebral fractures with subsequent wrist fractures was somewhat weaker (RR = 1.4) than for other subsequent fracture types. In the five studies that examined the effect of adjusting for BMD,[33,34,36–38] the magnitude of association was reduced by 20% or less (Appendix 2). Conversely, BMD remained a strong predictor of fracture independent of prior fractures (data not shown); BMD and prior fractures complement each other for predicting fracture risk.

The strongest association was with subsequent vertebral fractures—approximately 2 times greater (RR = 4.4) than for subsequent fractures at other sites among postmenopausal women, and much greater (RR = 19.0) for other populations (Table 1). Other studies also reported strong associations between prior and subsequent vertebral frac-

tures, but the categories of number of prior fractures that were reported precluded pooling across studies.[35–37,39] Three studies reported that the risk of subsequent vertebral fractures increased dramatically with increasing number of prevalent fractures at baseline.[36,37,53] For example, the odds of a new vertebral fracture among women with five or more vertebral fractures at baseline was 35 times greater than for women without vertebral fractures at baseline.[37]

Excluding the studies of subsequent vertebral fractures, the associations of prior vertebral fractures with subsequent fractures (of all types) were similar for peri-/postmenopausal women (pooled RR = 1.9) compared with other studies (RR = 2.3; Table 1).

Prior fractures of any type

There were 19 reports of associations between fractures at any skeletal site (or specific sites other than spine, hip, or wrist) and subsequent fractures (Appendix 2). Twelve of the publications were based on prospective studies.[11,14,23,26,27,30,35,39,41–44] As with prior wrist fractures, the remaining reports included case-control studies and cross-sectional mail surveys.[17,19,38,45–48] Some of the studies involved only men,[14,43,48] whereas others included men and women.[38,45,46] As noted in Appendix 2, some studies excluded almost half of prior fracture cases, and the validity of other studies was uncertain, but all publications were included when calculating the pooled estimates, except one that did not provide 95% CI.[35]

Several studies involved perimenopausal women,[26,27] or prior fractures that occurred before age 50.[45,47] The associations with subsequent fractures of all types in these studies (RR = 1.4 to 2.8) were of similar magnitude to other studies that involved postmenopausal women (RR = 1.3 to 3.1).[11,17,35,38,44]

Among studies of peri-/postmenopausal women, pooled estimates were remarkably uniform for all fracture categories, with relative risks between 1.8 and 2.0 (Table 1). For other studies, associations were stronger for subsequent hip fractures (RR = 2.1) than for all subsequent fractures (RR = 1.4). Pooled RR estimates for all fracture types combined were slightly greater for peri-/postmenopausal women (RR = 1.9) compared with other studies (RR = 1.7).

Only one study examined associations for multiple prior fractures; the risk of subsequent fractures was increased by 5.9 times among women with two or more prior fractures.[26] This large increase in risk among women with multiple fractures suggests that the number of fractures may be more important than the location of prior fractures.

One case-control subset analysis found that history of prior fracture was associated with reduced risk of hip fracture.[49] However, this study was omitted from the appendices because of the unusual nature of the sample; the subset involved only men who had hip fracture that resulted from a fall and men without hip fractures who had fallen in the past year.

Prior hip fractures

Six publications reported associations between prior hip fractures and subsequent fractures (Appendix 2). One involved men only,[24] and one included both men and women;[50] the others involved only women.[17,18,22,42] The mean age was 70 years or older in most studies. Most studies were either cohort design or compared the incidence of new fractures among people with prior hip fractures to the incidence in the community. The magnitudes of associations did not vary appreciably by location of subsequent fractures and were similar to those for other prior fracture types (Table 1). The association was somewhat stronger for subsequent morphometric vertebral fractures (RR = 2.5), but there was only one such study; this study also adjusted for several covariates.[42] For other studies, the pooled estimate (RR = 1.7) was smaller than the estimate for peri-/postmenopausal women (RR = 2.4).

Pooled estimates for subsequent fracture types and for all combinations of prior and subsequent fractures

The pooled-column estimates in Table 1 allow comparison of associations for prior fractures at any site by location of subsequent fractures. Among peri-/postmenopausal women, associations were remarkably uniform for all types of subsequent fractures, with relative risks ranging from 1.9 to 2.0. Among other studies, associations were similar in magnitude (relative to peri-/postmenopausal women), except that the association was greater for subsequent vertebral fractures (RR = 4.5). Accordingly, the pooled estimate for the entire table (excluding prior vertebral fracture predicting subsequent vertebral fracture) was similar for peri-/postmenopausal women compared with other studies.

DISCUSSION

We have identified numerous reports of increased risk of subsequent fractures among people with a history of fractures. Although the magnitude varied somewhat, the direction of association was very consistent among reports, and it is clear that there is an increased risk of future fracture among those who have already experienced a fracture. The risk of future fractures appears to increase with the number of prior fractures, especially for prior vertebral fractures predicting future vertebral fractures, but information for nonspine fractures is limited and deserves further study.

There appears to be some disagreement, even among experts, regarding associations between prior and subsequent fractures. For example, recent osteoporosis clinical guidelines[51] state that risk of new vertebral fracture is at least double among women with prior vertebral fractures, and prior wrist fracture is associated with triple the risk of future vertebral fracture and twice the future risk of hip fracture. Our summary suggests the associations of prior vertebral fractures with subsequent vertebral fractures are actually stronger, and associations of prior wrist fractures with subsequent vertebral fractures are weaker among postmenopausal women, than stated in the guidelines.

The pooled estimate in Table 1 suggests that peri-/postmenopausal women with prior fractures have twice the risk of future fractures overall (RR = 2.0), compared with those without prior fractures; the pooled estimate was similar for other studies (RR = 2.2). The sole exception was for prior spine fractures and subsequent spine fractures, for which the association is greater (RR = 4.4 to 19.0). Using all published studies to obtain pooled relative-risk estimates is a somewhat crude approach, which does not take into account advantages or disadvantages of individual study designs, or other potentially important factors. Despite the potential limitations, the associations are remarkably similar in direction and magnitude for all combinations of prior/subsequent fractures for which multiple reports were available (except as noted for prior/subsequent spine fractures).

The similarity of associations (in terms of direction and magnitude) for all sites, except prior vertebral fractures with subsequent vertebral fractures, suggests that a common mechanism may be involved. The associations were similar in magnitude, comparing studies of postmenopausal women with studies that considered fractures occurring before menopause, studies of perimenopausal women, and studies that included men. The increased risk may result, in part, from the fact that people who already had fractures also had low BMD. However, the studies that controlled for baseline BMD reported that adjusting for BMD reduced the magnitude of the association only slightly. This suggests that either a single measurement of BMD is not representative of overall skeletal status, or that prior fractures indicate the presence of mechanisms that influence risk, independent of current BMD.

Prior fractures may indicate defects in bone microarchitecture, a skeletal factor that may influence fracture risk, independent of BMD. Prior fractures might also indicate the presence of nonskeletal factors that increase fracture risk, such as increased frequency of falls or reduced protective responses. Nevertheless, BMD also remained a strong predictor of fracture risk after adjusting for prevalent fractures, indicating that both BMD and prevalent fractures contribute important, complementary information about fracture risk. A 1 standard deviation (SD) decrease has been associated with an approximate doubling of fracture risk in prospective cohort studies; the increase is somewhat greater for hip BMD predicting hip fracture (RR $\approx$ 2.5).[13,36,41,52,53] Thus, the increase in fracture risk among those with a prior fracture is similar in magnitude to that for 1 SD lower BMD. Furthermore, fracture risk increases progressively with greater decreases in BMD and with multiple prevalent fractures.

Prior vertebral fractures were strong predictors of future vertebral fractures, with a relative risk of ~4 for women with at least one vertebral fracture, and the risk increases approximately 2 to 4 times for each fracture present at baseline.[36,37,53] The larger magnitude compared with associations for nonspinal fractures may result because most spine fractures are attributable to bone fragility and often seem to occur spontaneously, whereas most nonspinal fractures are associated with falls or other minor trauma. Prior vertebral fracture alone is a strong risk factor for hip fracture as well as other osteoporotic fractures in both peri- and postmenopausal women and other populations. Even a small increase in relative risk is important because of the costs related to hip fractures—an average of $21,000 per patient for direct medical care.[54]

Some evidence suggests that initial fractures that occur earlier in life signal a higher subsequent risk of fracture than fractures that occur later in life,[50,55] although this may not apply to all types of fractures.[25]. Fracture at an early age partly represents low BMD, and there will be many years of additional bone loss, which will increase risk further. Most women with a history of low trauma fractures have low BMD, and women with both low BMD and prior fractures have very high risk of future fractures.[13] Therefore, an important clinical goal is to prevent the bone loss that leads to the first fracture, because this bone loss is largely irreversible by the time the first fracture occurs. Nevertheless, it is important to treat women who have already experienced fractures, as well as those with low BMD who have not yet fractured. Effective treatments are available that can reduce risk by half, whether or not fractures have already occurred.[35] Prior fractures indicate an increased risk of future fractures, and fracture risk will continue to increase progressively if left untreated, resulting in multiple fractures, and a high risk of devastating hip fractures. Although the association between prior fracture and future fracture is well established in the current literature, it appears that few elderly patients who have experienced recent fractures are receiving treatment to prevent future fractures.[56–59]

Potential limitations of this study

The literature review may have missed some reports that examined associations of prior fractures with subsequent fractures; however, it seems unlikely that major reports would have been missed. Furthermore, given the consistency of results found among the reports summarized here, it seems unlikely that any studies inadvertently omitted would alter the conclusions (i.e., that they would find strong associations in the opposite direction).

Conclusion

The evidence clearly indicates that history of any prior fracture is an important risk factor for future fractures, including costly and disabling hip and vertebral fractures. Older patients who present with fractures should be regarded as having an increased risk of developing future fractures, and should receive further evaluation for osteoporosis as well as risk for hip and other fractures.

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Address reprint requests to:
Carolyn M. Klotzbuecher
Merck & Co., Inc., WP39-160
Sumneytown Pike
West Point, PA 19486 U.S.A.

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Appendix 1. Published Relative Risk Estimates and Confidence Intervals Used to Calculate the Pooled Estimates Shown in Table 1

Location of prior fracture	*Population*	*Location of subsequent fractures*			
		Wrist	*Vertebral*	*All (or nonspine)*	*Hip*
Wrist	Peri/postmenopausal	3.3 (2.0, 5.3)[19]	1.7 (1.4, 2.1)[17]	2.4 (1.7, 3.4)[19]	1.8 (1.3, 2.2)[23] 1.9 (1.5, 2.3)[17]
	Other	2.8 (2.2, 3.6)[25],[c] (Women)	5.2 (4.5, 5.9)[25] (Women)	1.8 (0.9, 3.6)[24] 1.5 (1.1, 2.1)[22]	1.4 (1.1, 1.8)[20] 1.5 (1.2, 1.9)[21] (Women)
		2.1 (1.4, 2.9)[25] (Women)[d]	10.7 (6.7, 16.3)[25] (Men)	2.0 (1.8, 2.2)[25] (Women)	2.3 (1.2, 4.5)[21] (Men) 1.4 (1.1, 1.9)[25] (Women)
		2.6 (0.7, 6.5)[25],[c] (Men)		2.5 (1.9, 3.1)[25] (Men)	2.7 (1.0, 5.8)[25] (Men)
		24.1 (6.6, 61.7)[25] (Men)[d]			
Vertebral	Peri/postmenopausal	1.4 (1.2, 1.7)[33]	4.8 (3.9, 6.0)[33],[a,b] 3.9 (2.9, 5.2)[17]	1.8 (1.6, 1.9)[33],[a] 1.8 (1.5, 2.2)[34],[a]	3.8 (1.8, 7.1)[30] 2.2 (1.8, 2.7)[33],[a] 2.6 (1.5, 4.5)[34],[a] 2.4 (1.6, 3.5)[17]
	Other	1.4 (1.0, 1.8)[31] 3.3 (0.4, 12)[29] (Men)	33 (24, 43)[29] (Men) 11.1 (9.7, 13)[29]	1.5 (1.3, 1.8)[31] 2.2 (1.4, 3.4)[22]	1.7 (1.3, 2.2)[31] 1.8 (1.3, 2.4)[32]
		1.5 (0.9, 2.3)[29] (Women)	(Women)	4.4 (1.5, 13.3)[38],[a]	4.7 (2.3, 8.7)[29] (Men)
				3.7 (1.6, 8.9)[24] 4.2 (3.2, 5.3) (Men)[29] 2.7 (2.4, 3.0)[29] (Men)	2.1 (1.6, 2.7)[29] (Women)
Other (all, or specific sites)	Peri/postmenopausal	2.3 (1.1, 4.6)[27] 1.7 (1.2, 2.3)[44]	1.4 (1.0, 2.0)[42],[b] 2.2 (0.8, 5.7)[39],[b] 2.3 (2.0, 2.7)[17]	2.4 (1.6, 3.7)[26] 2.8 (2.0, 4.1)[27] 1.4 (1.0, 1.8)[11] 1.4 (0.9, 2.2)[44]	2.4 (1.3, 4.0)[30] 2.5 (1.3, 3.6)[23] 1.5 (1.1, 2.0)[41] 1.9 (1.6, 2.3)[19] 2.2 (1.6, 2.6)[17]
	Other	—	—	1.7 (1.3, 2.3)[45] 1.4 (1.2, 1.6)[47] 3.1 (1.1, 8.6)[38] 1.2 (1.1, 1.3)[14]	3.6 (1.1, 12.2)[47] 1.2 (0.7, 1.9)[46] 2.7 (1.8, 3.6)[23] 1.0 (0.5, 2.0)[43] 3.7 (2.2, 6.2)[48]
Hip	Peri/postmenopausal	—	2.5 (1.1, 6.0)[42],[b] 2.5 (1.9, 3.9)[17]	1.9 (NA)[18],[e]	2.3 (1.5, 3.7)[17]
	Other	—	—	2.4 (1.3, 4.6)[22] 1.6 (1.0, 5.4)[24]	1.6 (1.3, 1.9)[50]

[a] Prior vertebral fractures were diagnosed using morphometry in these studies; prior vertebral fractures were clinically diagnosed in all other studies in the "prior vertebral fracture" row.

[b] New vertebral fractures were diagnosed using morphometry in these studies; new vertebral fractures were clinically diagnosed in other studies.

[c] Prior wrist fracture occurred before age 70.

[d] Prior wrist fracture occurred after age 70.

[e] NA = no CI reported.

APPENDIX 2. DESCRIPTIONS AND RELATIVE RISK ESTIMATES FROM PUBLISHED STUDIES, BY LOCATIONS OF PRIOR AND SUBSEQUENT FRACTURES

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Wrist							
Distal radius[23]	1162 F 20–99 yr with prior wrist frx; population-based sample	Compared incidence of new hip frx (n = 49) among cases to age- & sex-specific expected incidence in the same community using population-based medical records data	4.0 yr	—	—	**1.8** (1.3, 2.2)	Some previous frx may not be representative of osteoporotic frx.
	F 60–79 yr with prior wrist frx; population-based sample	Age 60–79 yr subset; 31 new hip frx		—	—	1.9 (1.3, 2.6)	See above.
Wrist[19]	12,162 F 47–57 yr; 144 had wrist frx at age 20–34	Cross-sectional postal survey; outcome = wrist frx at age 35–57 (n = 17)	NA	—	**3.3** (2.0, 5.3) [wrist only]	—	Includes pre- and early postmenopausal. Previous frx are not representative of osteoporotic frx.
	Same as above	See above; outcome = nonwrist frx at age 35–57 (n = 30)	NA	—	**2.4** (1.7, 3.4) [nonwrist]	—	Includes pre- and early postmenopausal. Previous frx are not representative of osteoporotic frx.
Colles[20]	350 F & 44 M with Colles' frx between 1945–1959; population-based sample	Compared age- & sex-specific incidence of new hip frx among cases (n = 54) to expected incidence in the same community using population-based medical records data	6145 pt-yr	—	—	**1.4** (1.1, 1.8)	Men & women combined
	350 F only	See above; 47 hip frx		—	—	1.3 (0.9, 1.7)	Women only
	344 F & 36 M excluding violent Colles' frx	See above; 53 hip frx		—	—	1.5 (1.1, 1.9)	Men & women
Distal forearm[21]	1126 F & 212 M ages 40+, with distal forearm frx between 1968–1972; population-based sample	Compared to 1126 F & 212 M age- & sex-matched controls; population-based sample	40,832 pt-yr (follow-up through 1991); 365 new hip frxs	—	—	F: **1.5** (1.2, 1.9) M: **2.3** (1.2, 4.5)	
Distal forearm[22]	1076 F; 259 age < 50, 530 age 50–69, 287 age > 70 yr; 283 with distal forearm frx	Prospective (cohort). Outcome = fragility frx at proximal humerus, distal radius, vertebra, pelvic rami, hip, or tibial condoyle from 1975 to 1985 (n = 258 F).	11 yr	—	**1.5** (1.1, 2.1)	—	

(*Appendix continues*)

APPENDIX 2. (CONTINUED)

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Distal radius[18]	490 F ages 45 or older with a distal radius frx in 1981; mean age = 66 yr	Prospective. Frxs at any site after 1981 (n = 75 F) were identified by mail survey. Frx rate compared to population-based data for F of same age	6 yr	—	2.1 (CI not given)	—	May not be adjusted adequately for age
Distal radius[24]	654 M with prior BMD measurements; 82 had prior distal radius frxs	Population-based review of all subsequent radiographs; outcome = fragility frx at proximal humerus, distal forearm, vertebra, pelvic rami, hip, or tibial condoyle from 1975 to 1985 (n = 165 new frx in 111 men)	11 yr	—	**1.8** (0.9, 3.6)	—	Men only
Forearm[25]	243 men, 1045 women ages 35 with prior distal forearm frx	Compared incidence of new frx among cases to age- & sex-specific expected incidence in the same community using population-based medical records data	548 patients had new frx during 9664 pt-yr follow-up; 104 forearm, 249 vertebral, 78 hip	—	**2.8** (**women**) (2.2, 3.6) **2.6** (**men**) (0.7, 6.5)	—	New wrist frx only; prior wrist frx before age 70
					2.1 (**women**) (1.4, 2.9) **24.1** (**men**) (6.6, 61.7)		New wrist frx only; prior wrist frx after age 70
				5.2 (4.5, 5.9) **10.7** (6.7, 16.3)	**2.0** (1.8, 2.2) **2.5** (1.9, 3.1)	**1.4** (1.1, 1.9) **2.7** (1.0, 5.8)	Women Men
Wrist[17]	29,802 women ages 50–80	Cross-sectional postal survey; outcome = frx within prior 10 years. N = 7164 wrist frx, 1196 hip frx, 1703 spine frx (including both new and prior frx)	NA	**1.7** (1.4, 2.1)	—	**1.9** (1.5, 2.3)	

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Spine							
Vertebral (clinical)[31]	186 M & 495 F with first vertebral frx diagnosis at age < 70 yr between 1950–1989	Compared incidence of new frx among cases to age- & sex-specific expected incidence in the same community using population-based medical records data	8,342 pt-yr; 57 F & 1 M new hip frxs	—	—	**1.7** (1.3, 2.2)	RR = 1.8 (1.3, 2.4) excluding previous violent vertebral frx
	Same as above	Same as above	Same, but 43 F & 5 M new distal forearm frxs	—	**1.4** (1.0, 1.8) [distal forearm]	—	RR = 1.5 (1.0, 2.0) excluding previous violent vertebral frx
	Same as above	Same as above	Same, but 58 F & 13 M new proximal humerus frx	—	4.5 (3.5, 5.7) [proximal humerus]	—	
	Same as above	Same as above	Same, but 249 F & 44 M new limb frx	—	**1.5** (1.3, 1.8) [any limb]	—	RR = 1.6 (1.3, 2.0) excluding previous violent vertebral frx
Lumbar spine (clinical)[30]	70 F age 59+ with frx between 1976–1984	Compared incidence of new hip frx (n = 10) among cases to age- & sex-specific expected incidence in the same community using population-based medical records data	241 pt-yr	—	—	**3.8** (1.8, 7.1)	Previous frx may not all be representative of osteoporotic frx
Vertebral (clinical)[32]	336 F with first vertebral frx diagnosis at age 35–69 yr between 1950–1979, and no prior hip frx	Compared incidence of new hip frx (n = 52) among cases to age- & sex-specific expected incidence in the same community using population-based medical records data	4788 pt-yr	—	—	**1.8** (1.3, 2.4)	No difference in association for vertebral fractures before vs. after age 60 Previous frx may not all be representative of osteoporotic frx
Vertebral (morphometric)[34]	3013 F, age 65+; 20% had morphometric (3 SD) vertebral frx at baseline	Prospective (cohort)	2.9 yr; 454 new nonpine frx, including 56 new hip	—	**1.8** (1.5, 2.2) [nonspine]	**2.6** (1.5, 4.5)	Age-adjusted
	Same	Same	Same	—	1.7 (1.4, 2.1) [nonspine]	2.2 (1.3, 3.8)	Adjusted for age & BMD

(*Appendix continues*)

APPENDIX 2. (CONTINUED)

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Vertebral (clinical)[22]	1076 F; 259 age < 50, 530 age 50–69, 287 age > 70 yr; 87 with prior vertebral frx.	Prospective (cohort). Outcome = fragility frx at proximal humerus, distal radius, vertebra, pelvic rami, hip, or tibial condoyle from 1975 to 1985 (n = 555 frx in 258 women)	11 yr	—	**2.2** (1.4, 3.4)	—	
Vertebral (morphometric)[33]	7238 F, age 65+; 20% had morphometric (3 SD) vertebral frx at baseline	Prospective (cohort). N = 389 women with new vertebral frx, defined as >20% decrease in vertebral height; n = 2433 women with new nonvertebral frx	3.7 yr for vertebral frx, 8.3 yr for nonvertebral frx	**4.8** (3.9, 6.0)	**1.8** (1.6, 1.9)	**2.2** (1.8, 2.7)	Age-adjusted
				4.1 (3.3, 5.1)	1.6 (1.5, 1.8)	1.9 (1.5, 2.3)	Adjusted for age & BMD
				3.8 (3.1, 4.7)	1.5 (1.4, 1.6)	1.7 (1.4, 2.1)	Adjusted for age, BMD, & other variables
Two or more morphometric frx[35]	1005 F age 55–81 yr in placebo arm of a clinical trial with at least one morphometric vertebral frx and low femoral neck BMD (T-score < −1.6).	Prospective (cohort) New vertebral frx defined as >20% (and >4 mm) decrease in vertebral height	2.9 yr	3.2	1.5	—	Compared to women with a single morphometric vertebral frx Not adjusted for age
Vertebral (morphometric)[39]	1098 F age 43–80; 83 had prevalent vertebral frx and 103 had prior nonspine frx.	Prospective (cohort); 63 new vertebral frx cases	4.7 yr	4.2 (2.2, 8.0)	—	—	Adjusted for age, prior nonspine fractures (only), prior spine plus nonspine fractures, and spine BMD
Vertebral (morphometric) *plus* nonspine[39]	Same	Same	Same	3.4 (1.0, 11.6)	—	—	Adjusted for age, prior nonspine fractures (only), prior spine fractures (only), and spine BMD
Vertebral (morphometric)[36]	893 F, age 43–80; 83 had morphometric (3 SD) crush or wedge vertebral frx at baseline	Prospective (cohort) Incident frx defined as 15+% decrease in vertebral height (n = 61) Adjusted for age	4.7 yr				
Single crush frx				5.3 (1.9, 15.2)	—	—	
Single wedge frx				4.1 (2.1, 8.1)	—	—	

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
2 or more crush or wedge frx				11.8 (5.1, 26.8)	—	—	
Vertebral (radiographic)[37]	380 F in a clinical trial; mean age = 65 yr Semiquantitative frx diagnosis; 287 had frx at baseline	Prospective; 47 new vertebral frx	2.9 yr				
1–2 frx				7.4 (1.0, 55.9)	—	—	Adjusted for age, treatment, 3–4 frx, and 5+ frx at baseline
3–4 frx				25.8 (3.4, 194.6)	—	—	Adjusted for age, treatment, 1–2 frx, and 5+ frx at baseline
5+ frx				34.6 (4.6, 257.6)	—	—	Adjusted for age, treatment, 1–2 frx, and 3–4 frx at baseline
Vertebral (morphometric)[38]	35 F & 4 M cases with new non-spine frx and 210 controls; mean age = 75 yr All had spine radiographs at baseline	Nested case-control (1:4). Mild spinal deformity was present in 119 people, and severe deformity in 24.	1.7 yr				Adjusted for age & sex
Mild		Mild spinal deformity = 1 to 3 vertebra with height ratios 2 to 3 SD below the mean (grade I), or a single vertebra with height ratio more than 3 SD below the mean (grade II)		—	1.6 (0.7, 3.5) [non-spine]	—	RR = 1.5 (0.6, 3.4) after additional adjustment for BMD
Severe		Severe spinal deformity = more than 3 grade I or more than one grade II deformities		—	**4.4** (1.5, 13.3) [non-spine]	—	RR = 4.1 (1.3, 12.4) after additional adjustment for BMD
Vertebral (clinical)[24]	654 M with prior BMD measurements; 31 had prior vertebral frxs	Population-based review of all subsequent radiographs; outcome = fragility frx at proximal humerus, distal forearm, vertebra, pelvic rami, hip, or tibial condoyle from 1975 to 1985 (n = 165 new frx in 111 men)	11 yr		**3.7** (1.6, 8.9)		Men only

(*Appendix continues*)

APPENDIX 2. (CONTINUED)

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Spine (clinical)[17]	29,802 women ages 50–80	Cross-sectional postal survey; outcome = frx within prior 10 years. N = 7164 wrist frx, 1196 hip frx, 1703 spine frx (including both new and prior frx)	NA	**3.9** (2.9, 5.2)	—	**2.4** (1.6, 3.5)	
Vertebral (clinical)[29]	151 men, 589 women ages ≥ 35 yr with prior clinical vertebral frx	Compared incidence of new frx among cases to age- & sex-specific expected incidence in the same community using population-based medical records data	432 patients (all ages) had 896 new frx during 4349 pt-yr follow-up; 34 distal forearm, 398 vertebral, 96 hip	**33** (24, 43)	**4.2** (3.2, 5.3)	**4.7** (2.3, 8.7)	Men
				11.1 (9.7, 13)	**2.7** (2.4, 3.0)	**2.1** (1.6, 2.7)	Women
Vertebral (morphometric)[53]	6082 F age 55–81 yr in a clinical trial with low femoral neck BMD (T-score < −1.6)	Prospective (cohort) 344 women had new vertebral frx defined as >20% (and >4 mm) decrease in vertebral height	3.8 yr	Placebo group 3.0 (2.2, 4.1) Alendronate 2.9 (1.9, 4.3)	—	—	Women with prior vertebral frx had 1.4 yr shorter follow-up—therefore, analysis probably underestimates association, and was not pooled with other studies. Adjusted for age, weight, BMD.
Other							
Single prior frx[26]	1857 F, age 45–49 at baseline; population-based sample	Prospective (cohort); postal survey 2 yr after baseline examination; 44 new frx.	2 yr	—	**2.4** (1.6, 3.7)	—	Previous and incident frx are not all representative of osteoporotic frx. RR = 2.1 (1.0, 4.3) adjusted for age & BMD
2+ prior frxs				—	5.9 (2.6, 3.4)	—	RR = 4.0 (1.7, 9.5) adjusted for age & BMD
Any frx in prior 10 yr[27]	3014 F age 47–56 (mean = 53 yr); population-based sample	Prospective (cohort). Outcome = any nonviolent frx (n = 157), including wrist (n = 42)	2.4 yr	—	**2.8** (2.0, 4.1) [all frxs] **2.3** (1.1, 4.6) [wrist only]	—	Previous and incident frx are not all representative of osteoporotic frx

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Tibia or ankle[45]	317 M & 174 F with tibial shaft frx between 1949–1963 (mean age at frx = 29), or ankle frx between 1961–1965 (mean age at frx = 38 yr); 51% of tibia and 15% of ankle frx were due to violent force Population-based sample.	Compared to double sex- and age-matched controls; population-based sample. Outcome = fragility frx at proximal humerus, distal radius, vertebra, pelvic rami, hip, or tibial condoyle prior to 1992 (n = 215)	Not given	—	**1.7** (1.3, 2.3)	—	Previous frx are not representative of osteoporotic frx. Sample represents only about one-third of all patients with prior fractures—remainder were lost to follow-up
Any frx before age 50[47]	7459 F born between 1900–1940; only 4223 analyzed, of which 268 had frx prior to age 50	Cross-sectional postal survey; outcome = frx after age 50 (n = 1132)	NA	—	**1.4** (1.2, 1.6)	—	Previous frx may not be representative of osteoporotic frx. Analyses may be suspect: only 4223 women were included in analyses, results of a poorly-defined "control group" are reported separately, and it is not clear if the analyses accounted adequately for possible differences in age and time at risk
Any frx after age 30	Same, but number with prior frx not available	Same, but outcome = "hip frx later in life"		—	—	**3.6** (1.1, 12.2)	See above
Any previous fracture[46]	246 hip fracture cases; F & M, mean 80 yr (F) and 74 yr (M). Excluded if institutionalized, poor cognition, or violent hip fracture	Case control; 246 age- & sex-matched controls	1 yr	—	—	**1.2** (0.7, 1.9)	About half of all hip fracture cases (n = 225) were excluded, leaving only 246
Any frx between age 20–34[19]	12,162 F 47–57 yr; 553 had frx at age 20–34	Cross-sectional postal survey; outcome = frx at age 35–57 (n = 1782)	NA	—	—	**1.9** (1.6, 2.3)	Includes pre- and early postmenopausal women Previous frx are not representative of osteoporotic frx

(*Appendix continues*)

APPENDIX 2. (CONTINUED)

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Olecranon[30]	52 F age 59+ with frx between 1976–1984	Compared incidence of new hip frx (n = 5) among cases to age- & sex-specific expected incidence in the same community using population-based medical records data	180 pt-yr	—	—	2.6 (0.9, 6.1)	Previous frx may not all be representative of osteoporotic frx Low power (0.44) for prior olecranon frx
Knee	129 F age 59+ with frx between 1976–1984	Same as above, but 14 new hip frxs	469 pt-yr	—	—	**2.4** (1.3, 4.0)	See above
Ankle	200 F age 59+ with frx between 1976–1984	Same as above, but 8 new hip frxs	779 pt-yr	—	—	1.3 (0.6, 2.7)	See above. Low power (0.12) for prior ankle frx
Proximal humerus[23]	406 F 20–99 yr with proximal humerus frx	Compared incidence of new hip frx among cases (n = 32) to age- & sex-specific expected incidence in the same community using population-based medical records data	3.7 yr	—	—	**2.7** (1.8, 3.6)	Previous frx may not be representative of osteoporotic frx
Proximal humerus	F 60–79 yr	Subset of study above; 16 new hip frx	3.7 yr	—	—	**2.5** (1.3, 3.6)	See above
Any frx since age 50[41]	9516 F age 65+	Prospective (cohort); 192 new hip frxs	4.1 yr	—	—	**1.5** (1.1, 2.0)	Adjusted for age, bone density, and 14 other covariates
Non-hip frx[42]	5822 F age 65+ without vertebral fractures at baseline	Prospective (cohort). New frx defined as 20+% decrease in vertebral height (n = 181)	3.7 yr	**1.4** (1.0, 2.0)	—	—	Adjusted for daily milk consumption during pregnancy, weight gain since age 25, maternal history of wrist fractures, age, prior hip frx, and smoking
Non-hip frx[43]	2879 M age 45 or older	Prospective (cohort); 71 new hip frx	39,914 p-yr	—	—	**1.0** (0.5, 2.0)	Men only. Adjustment for covariates including BMD had no effect

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Frx since age 45[35]	1005 F age 55–81 yr in placebo arm of a clinical trial with at least one morphometric vertebral frx and low femoral neck BMD (T-score < −1.6).	Prospective (cohort); 183 new clinical frx, 145 new morphometric vertebral frx cases	2.9 yr	1.4 (CI not given)	1.3 (CI not given) [clinical frx]	—	All women had low BMD and at least one morphometric vertebral frx. Not adjusted for age
Wrist or hip[38]	35 F & 4 M cases with new nonspine frx and 210 controls; mean age = 75 yr.	Nested case-control (1:4)	1.7 yr	—	**3.1** (1.1, 8.6)	—	Adjusted for age & sex
Nonspine frx only (no spine frx)[39]	893 F age 43–80; 83 had prevalent vertebral frx and 103 had prior nonspine frx.	Prospective (cohort); 63 new vertebral frx cases	4.7 yr	**2.2** (0.8, 5.7)	—	—	Adjusted for age, prior spine fractures (only), prior spine plus nonspine fractures, and spine BMD
Any frx (since age 50?)[11]	9704 F age 65 or older; 37% had prior frxs; population-based sample	Prospective (cohort)	5.9 yr				
		Outcome = new frx of ankle (191 women)		—	Not significant	—	New ankle frx only
		Outcome = new frx of foot (204 women)		—	**1.4** (1.0, 1.8)	—	New foot frx only
Any frx since age 50[44]	9704 F age 65 or older; 37% had prior frxs; population-based sample	Prospective (cohort)	2.2 yr				
		Outcome = new frx of distal forearm (171 women)		—	**1.7** (1.2, 2.3) [wrist]	—	New distal forearm frx only Not adjusted for age Not significant after adjustment for covariates (adjusted RR = 1.3)
		Outcome = new frx of proximal humerus (79 women)		—	**1.4** (0.9, 2.2) [humerus]	—	New proximal humerus frx only
Any frx in prior 5 yrs[14]	820 M age 60 or more; 752 had baseline BMD measurements.	Prospective (cohort); 166 new atraumatic frxs	5 yr	—	**1.2** (1.1, 1.3)	—	Men only. R = 1.4 (1.2, 1.5) after adjusting for BMD

(*Appendix continues*)

APPENDIX 2. (CONTINUED)

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Distal forearm, proximal humerus, pelvis, or vertebra[48]	232 M ages 35+ with hip frx between 1965–1989, excluding pathologic or violent frx; mean age 79 yr. Population-based sample; 84 M had prior forearm, spine, pelvis, or humerus frx	Case control; 232 M controls without hip frx.	37 yr	—	—	**3.7** (2.2, 6.2)	Men only
Wrist, hip, humerus, or spine[17]	29,802 women ages 50–80	Cross-sectional postal survey; outcome = frx within prior 10 years. N = 7164 wrist frx, 1196 hip frx, 1703 spine frx (including both new and prior frx)	NA	**2.3** (2.0, 2.7)	—	**2.2** (1.6, 2.6)	
Hip							
Hip[50]	914 F (mean 75 yr) & 231 M (mean 71 yr) with prior hip fracture; population-based sample	Compared age- and sex-specific incidence of new hip frx (n = 106) among cases to expected incidence in the same community using population-based medical records data	10,441 pt-yr	—	—	**1.6** (1.3, 1.9)	For all hip fractures
	F & M	Subanalysis of study above	99 new frx	—	—	1.8*	Excludes first hip fractures from severe trauma
	M only		11 new frx			3.2*	
	F only		88 new frx			1.7*	
	Frx before age 60 (F & M)	Subanalysis of study above, analyzed by age group	11 new frx	—	—	3.9‡	Excludes first hip fractures from severe trauma
	Frx at ages 60–69 (F & M)		24 new frx			3.0‡	
	Frx at age 70+ (F & M)		64 new frx			1.4†	
Hip[42]	5822 F age 65+ without vertebral fractures at baseline	Prospective (cohort). New frx defined as 20+% decrease in vertebral height (n = 181)	3.7 yr	**2.5** (1.1, 6.0)	—	—	Adjusted for daily milk consumption during pregnancy, weight gain since age 25, maternal history of wrist fractures, age, prior non-hip frx, and smoking

Prior fracture location	*Study population*	*Study design*	*Follow-up*	*Vertebral fracture*	*All fractures*	*Hip fracture*	*Comments*
Trochanteric hip frx[22]	1076 F; 259 age < 50, 530 age 50–69, 287 age > 70 yr; 40 F with prior trochanteric hip frx	Prospective (cohort) Outcome = fragility frx at proximal humerus, distal radius, vertebra, pelvic rami, hip, or tibial condoyle from 1975 to 1985 (n = 555 new frx in 258 women).	11 yr	—	**2.4** (1.3, 4.6)	—	
Hip[24]	654 M with prior BMD measurements; 39 had prior hip frxs	Population-based review of all subsequent radiographs; outcome = fragility frx at proximal humerus, distal forearm, vertebra, pelvic rami, hip, or tibial condoyle from 1975 to 1985 (n = 165 new frx in 111 men)	11 yr		**1.6** (1.0, 5.4)		Men only
Hip frx in 1981[18]	432 F ages 45 or older with a hip frx in 1981; mean age = 80 yr	Prospective. Frxs at any site after 1981 (n = 31 hip, 24 other frx) were identified by mail survey. Frx rate compared to population-based data for F of same age	6 yr	—	**1.9** (CI not given)	—	May not be adjusted adequately for age. Also, mortality was 67% during 6 yrs after the initial hip frx
Hip[17]	29,802 women ages 50–80	Cross-sectional postal survey; outcome = frx within prior 10 years. N = 7164 wrist frx, 1196 hip frx, 1703 spine frx (including both new and prior frx)	NA	**2.5** (1.9, 3.9)	—	**2.3** (1.5, 3.7)	

Studies involved postmenopausal women, except as otherwise noted. RR values shown in bold were used to compile the results in Table 1 and Appendix 1.
F, female; M, male; frx, fracture; yr, year(s); NA, no CI available.
* $P < 0.05$; † $P < 0.01$; ‡ $P < 0.001$.